In the specification:

Replace the original Sequence Listing with the substitute Sequence Listing filed herewith.

Amend the paragraph beginning at page **54**, line **4**, as follows:

Durst and Nelson (1995) *Drug Metab. Drug Interact.* 12:189-206 classified plant cytochrome P450s into two distinct groups based on their clustering nature in a phylogenetic tree. All of the group A families cluster and are assumed to originate from a common plant P450 ancestor. The group A cytochrome P450s conform to the characteristic consensus sequences (A/G)GX(D/E)T(T/S) in domain A (also called helix I) and PFG(A/S/V)GRRXC(P/A/V)G (SEQ ID NO:26) of the heme binding domain (D) with only a few exceptions. Group A cytochrome P450s appear to catalyze plant-specific reactions such as lignin biosynthesis (Figure 6; GenBank accession number P48421). By contrast, P450s that do not belong to group A (non-A P450s) are scattered in the phylogenetic tree. They share more amino acid identity/similarity with P450s found in animals, microbes, and fungi than with those found in plants. The non-A P450s possess functions, such as steroid metabolism, that are not limited to plants. Generally, non-A P450s have limited homology with known domains described for group A.

Amend the paragraph beginning at page **55**, line **1**, as follows:

Six cytochrome P450 sequences with the greatest homology to DWF4, CYP90A1, CYP85, CYP88 (Winkler and Helentjaris (1995) *Plant Cell* 7:1307-1317; GenBank accession number U32579), cyanobacteria CYP120 (Kaneko et al. (1996) *DNA Res.* 3:109-136; GenBank accession number D64003), human CYP3A3X (Molowa et al. (1986) *Proc. Natl. Acad. Sci.* USA 83:5311-5315; GenBank accession number M13785), and zebrafish CYP26 (White et al. White (1996) *J. Biol. Chem.* 271:29922-29927; GenBank accession number U68234), were chosen for multiple sequence alignment. Putative domains defined by Kalb and Loper (1988), *supra* are boxed and labeled in Figure 3. First, the heme binding domain pFGgFpRlCpGkel (SEQ ID NO:27) matches completely the sequence defined previously. Uppercase letters in the domain indicate amino acids conserved at all seven sequences in the alignment, and lower-case

letters represent residues conserved in at least half of the proteins. Of the amino acids conserved in the heme binding domain, the function of the cysteinyl is established as a thiolate ligand to the heme (Poulos et al. (1985), *supra*).

C2 cont.

[Amend the paragraph beginning at page **55**, line **15**, as follows:]

Domain A is defined by xllfaGhEttssxIxxa (SEQ ID NO:28). Lowercase x's indicate variable amino acids. An invariant glutamate (E) preceded threonine (T) at position 314, T314, which is believed to bind dioxygen, was conserved in all proteins compared except CYP88 of maize. The second signature sequence, domain B, is also conserved in *DWF4* with significant similarity. A valine at position 370 is conserved in all of the proteins, but is does not appear in Kalb and Loper's classic report (1988) on conserved domains. Again, DWF4 matches the domain C consensus sequence. Finally, the anchoring domain in the N-terminal end was distinguished by a repeat of the hydrophobic residue leucine. In addition, in DWF4, two acidic (glutamate) and two basic (histidine) residues precede the repeated leucine in the N-terminal leader sequence. These charged residues may add more stability to the membrane topology of the protein as a strong start-stop transfer peptide (von Heijne (1988) *Biochim. Biophys. Acta* 947:307-333).

[Amend the paragraph beginning at page **55**, line **28**, as follows:]

C3

Thus, phylogenetic analyses of these seven proteins with cytochrome P450s unique to plants (group A; Durst and Nelson (1995), *supra*) indicate that DWF4 does not cluster with these cytochrome P450s (Figure 4). Rather, DWF4 clustered with cytochrome P450s from other organisms: cyanobacteria (CYP120), rat (CYP3A2), human (CYP3A3X), and plants (CYP90, CYP85, and CYP88). DWF4 also deviates from the consensus sequence in the group A heme binding domain in that it possesses a PFGGGPRLCAG (SEQ ID NO:29) sequence in which arginine (R) is substituted for proline (P). However, domain A of DWF4, AGHETS (SEQ ID NO:30), fits the consensus of domain A of group A. These characteristics suggest that DWF4 is a monooxygenase, similar to P450s of group A, that utilizes molecular oxygen as a source of the hydroxyl group, but it mediates some reaction(s) that are not necessarily specific for plants, for instance, steroid hormone biosynthesis, which is a critical event for animals. In fact, the

C3 cont.

similarity of DWF4 to the rat testosterone 6β-hydroxylase (34%; GenBank accession number 631895) or glucocorticoid-inducible hydroxylase (31%; Molowa et al. 1986; GenBank accession number M13785) supports this idea. Further, the similarity that DWF4 shares with CYP90A and CYP85, 66 and 59%, respectively, is additional proof that it is involved in plant steroid biosynthesis (Bishop et al. 1996 ; Szekeres et al. 1996).